

## REMARKS

Claims 17 and 25-28 are pending in the instant application. Claims 17 and 25-27 have been amended. Support the amendments to claim 17 may be found in the specification, for example, at p. 15, l. 27-28; Example 4, in particular p. 24 l. 30-31; and p. 12, l. 15-17 which clearly states that granzyme B can be the only pharmaceutically active component in the composition. Support for new claim 29 may be found in the claims as originally filed and, for example, at page 13, lines 4-21, page 11, lines 18-24, page 1, lines 12-15 and in Example 4.

In the Office Action mailed October 12, 2007, the Examiner rejected the claims as follows:

1. Claims 17 and 25-27 are rejected under 35 USC §112, second paragraph as being indefinite;
2. Claims 17 and 28 are rejected under 35 U.S.C. §102(b) as being anticipated by Trouet I (WO 01/91798);
3. Claims 17 and 28 are rejected under 35 U.S.C. §102(e) as being anticipated by Trouet II (20040014652); and
4. Claims 17 and 25-28 are rejected under 35 U.S.C. §103(a) as being obvious over Trouet I or II.

In addition, Claim 17 is objected to because of informalities. Each rejection is addressed below.

### **1. Objection to the claims.**

The claims have been amended by adding “of,” “a” and reordering the Markush group to list tumor last.

### **2. The claims are definite.**

Claims 17 and 25-27 are rejected under 35 USC §112, second paragraph as being indefinite. Claim 17 has been amended to delete the allegedly indefinite claim language. Thus, the rejection is moot. Claims 25-27 have been amended to recite that the granzyme B is present in the pharmaceutical composition in a final concentration of 1µg/ml to 500µg/ml. Applicants respectfully submit that this amendment clarifies the claims and request that the rejection be withdrawn.

**3. The claims are novel.**

Claims 17 and 28 are rejected under 35 U.S.C. §102(b) as being anticipated by Trouet I (WO 01/91798) and under 35 U.S.C. §102(e) as being anticipated by Trouet II (20040014652). The disclosure of these two references is identical so the rejections are considered together. A claim is anticipated only if “each and every element as set forth in the claims is found, either expressly or inherently described, in a single prior art reference.” *Verdegaal Bros. v. Union Oil Co. Of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

The claims have been amended to specify that granzyme B is “isolated” and the only pharmaceutically active component in the pharmaceutical composition that is administered in the method. These claim elements are not taught by Trouet I or II. The Trouet application states:

“The biologically active entity may also be an entity that acts intracellularly but that is either incapable of traversing the cell membrane or does not efficiently traverse the membrane on its own...Intracellularly active agents that are not capable of traversing the cell membrane Include intracellularly active polypeptides such as granzyme B...”; see Trouet application at paragraph 0013 (emphasis added).

In paragraph 0140 the Trouet application went on to explain the killing effects of Granzyme B in that:

“This killing effect results from the synergistic effect of perforin, a membranolytic protein and the serine protease granzyme B...Perforin allows granzyme B to reach the cytoplasm and the nucleus of cells by inducing the formation of transmembrane pores that constitute a passage for the enzyme...In the prodrug, the transport peptide potentially plays the role of perforin by allowing granzyme B to enter the cell and to induce apoptosis.”

Thus, Trouet clearly teaches that an additional active component (in particular a transport peptide) besides granzyme B is required so that granzyme B can enter the cell. The Examiner’s reasoning regarding the rejection centers on the fact that the previously pending claims did not exclude prodrug forms. The claims as amended exclude prodrug forms of granzyme B. For these reasons, the invention as presently claimed is novel and Applicants requests that the rejection be withdrawn.

With respect to new claim 29 and the claims dependent thereon, Applicants note that the cited references do not teach the claim element of analyzing cells affected by said infection or

inflammation or tumor cells for surface expression of Hsp70. Thus, these claims are also novel in view of the cited prior art.

**4. The claims are not obvious.**

Claims 17 and 25-28 are rejected under 35 U.S.C. §103(a) as being obvious over Trouet I or II. A *prima facie* case of obviousness requires the Examiner to cite a combination of references which (a) disclose the elements of the claimed invention, (b) suggests or motivates one of skill in the art to combine those elements to yield the claimed combination, and (c) provides a reasonable expectation of success should the claimed combination be carried out. Failure to establish any one of these three requirements precludes a finding of a *prima facie* case of obviousness, and, without more, entitles Applicant to allowance of the claims in issue.<sup>1</sup> In addressing this rejection, Applicants focus on the independent claims since non-obviousness of an independent claim necessarily leads to non-obviousness of claims dependent therefrom.<sup>2</sup>

In the present case, any *prima facie* case of obviousness established by the Examiner is now rebutted by the amendments to the claims. In particular, Trouet does not teach or suggest the claim elements that specify that granzyme B is “isolated” and the only pharmaceutically active component in the pharmaceutical composition that is administered in the method. In fact, the passage from Trouet cited above teaches away from using granzyme B in isolation. The Examiner’s reasoning regarding the rejection centers on the fact that the previously pending claims did not exclude prodrug forms. The claims as amended exclude prodrug forms of granzyme B. Because the cited references do not teach or suggest each claim element, the *prima facie* case of obviousness stands rebutted and Applicant requests that the rejection be withdrawn.

With respect to new claim 29 and the claims dependent thereon, Applicants note that the cited references do not teach the claim element of analyzing cells affected by said infection or inflammation or tumor cells for surface expression of Hsp70. Thus, these claims are also non-obvious in view of the cited prior art.

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<sup>1</sup> See, e.g., *Northern Telecom Inc. v. Datapoint Corp.*, 15 USPQ2d 1321, 1323 (Fed. Cir. 1990).

<sup>2</sup> §MPEP 2143.03.

**Conclusion**

The Applicant believes the arguments set forth above traverse the Examiner's rejections and therefore request these alleged grounds for objection and rejection be withdrawn. Should the Examiner believe a telephone interview would aid in the prosecution of this application, the Applicant encourages the Examiner to call the undersigned collect.

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